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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/855,886	05/15/2001	Barry Coller	A31386-A	1518

21003 7590 06/30/2004

BAKER & BOTTS
30 ROCKEFELLER PLAZA
NEW YORK, NY 10112

EXAMINER	
HELMS, LARRY RONALD	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 06/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/855,886	COLLER ET AL	
	Examiner	Art Unit	
	Larry R. Helms	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-11 and 15-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5-11, 15-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 16-17 have been amended

2. Claims 1-3, 5-11, 15-17 are pending and under examination.

3. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.

Rejections Withdrawn

4. The rejection of claims 1-2 and 5-11 under 35 U.S.C. 112, first paragraph, is withdrawn in view of arguments.

Response to Arguments

5. The rejection of claims 1-3, 5-11, 15-17 under 35 U.S.C. 103(a) as being unpatentable over Max et al (Int. J. Cancer 71:320-324, 1997) in view of Taylor et al (Blood 89:4078-4084, 1997) and Mohle et al (PNAS 94:663-668, 1997) and Charo et al (J. Biol. Chem. 262:9935-38, 1987) as evidenced by Coller et al (Haemostasis 26:285-293, 1996) is maintained.

The response filed 4/19/04 has been carefully considered but is deemed not to be persuasive. The response states that in view of Max teaching the distribution of alphaVbeta3 on both endothelial and non-endothelial cell types in both normal and tumor samples, Max et al does not and cannot stand for the proposition that alphaVbeta3 expression is important in neovascularization of tumors and hence their

treatment by antagonist of alphaVbeta3 and further Max teaches that it is possible that alphaVbeta3 expression on normal vasculature does not serve any angiogenic function at all and thus, Max does not conclude a critical role for alphaVbeta3 in angiogenesis or tumor growth (see page 10 of response). In response to this argument, Max et al clearly teaches tumor tissues such as breast express alphaVbeta3 and as stated in the response alphaVbeta3 is in normal vasculature but does not contribute to angiogenesis in normal tissue, however, Max et al clearly realized that alphaVbeta3 was important for malignant angiogenesis and alphaVbeta3 antagonist could be used for treatment of tumors (see abstract and page 320).

The response further states that the teaching of Max et al relied upon by the examiner for tumors can be treated with alphaVbeta3 antagonist and angiogenesis contributes to diabetic retinopathy are not taught and are based on the Brooks et al papers and the response then addresses the teachings of Brooks et al (see pages 10-11 of response). In response to this it is not clear what Brooks teaching has to do with the rejection because none of the cited Brooks et al references are in the rejection. The response seems to argue that Max et al only teaches LM609 which lacks anti-GPIIb/IIIa binding and does not teach the combined antagonism of GPIIb/IIIa and alphaVbeta3 (see page 11 of response). In response to this argument, the rejection is a combination f references and as such the combination of references would teach antagonist of both GPIIb/IIIa and alphaVbeta3.

The response further states that Max et al does not teach a role for alphaVbeta3 in proliferative and inflammatory disorders and Brooks et al is the true source of the

teachings and teach away from treatment of these disorders with the use of anti-GPIIb/IIa antibodies (see page 12 of response). In response to this argument, again Brooks et al is not in the rejection and as such it is not clear what Brooks teaching has to do with the rejection.

The response further states that there would not have been motivation to extent the studies of Taylor et al to the treatment of proliferative disorders because there was no evidence implicating both alphaVbeta3 and GPIIb/IIIa in the process and no evidence that superior results would be obtained through the use of 7E3 relative to LM709 (see page 12 of response). In response to this argument, the motivation to use 7E3 also comes from the teachings of Mohle et al and Charo et al, which is not even addressed in the response, Mohle et al which teaches VEGF which is a potent angiogenic factor is overexpressed in tumors and VEGF is delivered by platelets and activated platelets release VEGF. Thus, in view of this one skill in the art would have been motivated to inhibit platelet aggregation which is known to occur and taught by Charo et al (see page 9935) through the GPIIb/IIIa. Thus, it would have been obvious to inhibit angiogenesis with an antagonist to both alphaVbeta3 and GPIIb/IIIa because both are implicated in angiogenesis and cancer by overexpression of VEGF by activated platelets wherein platelet activation is GPIIb/IIa dependent and alphaVBeta3 is implicated in tumors and treatment of tumors can be performed with alphaVbeta3 antagonist. Therefore, it would have been obvious to use an antagonist of both alphVbeta3 and GPIIb/IIIa and use the 7E3 antibody which obviously have the claimed properties of the antagonist.

Conclusion

6. No claim is allowed.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (571) 272-0832. The examiner can normally be reached on Monday through Friday from 6:30 am to 4:00 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ~~Christina Chan~~ Jeffrey S. Lu, can be reached on (571) 272-~~0841~~ 0787.

9. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the

Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

571-272-0832

LARRY R. HELMS, PH.D
PRIMARY EXAMINER